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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :		(11) International Publication Number: WO 90/09779
A61K 7/16, 7/22, C11D 3/48	A1	(43) International Publication Date: 7 September 1990 (07.09.90)

(21) International Application Number: PCT/US90/01041

(22) International Filing Date: 28 February 1990 (28.02.90)

(30) Priority data:
317,271 28 February 1989 (28.02.89) US

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(81) Designated States: AT (European patent), AU, BE (European patent), CA, CH (European patent), DE (European patent), DK, DK (European patent), ES (European patent), FI, FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), MC, NL (European patent), NO, SE (European patent).

Published
With international search report.

(54) Title: METHOD AND COMPOSITION FOR TREATMENT OF PERIODONTAL DISEASE

(57) Abstract

A composition for treatment of periodontal disease includes an aqueous carrier of sterile water, glycerin and ethanol in which are present chlorhexidine gluconate, allantoin, sodium salicylate and sodium bicarbonate. A preferred method of treatment includes topical application to human periodontium in a mouthwash.

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METHOD AND COMPOSITION FOR TREATMENT OF PERIODONTAL DISEASE

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to a method and composition for treatment of periodontal disease and, more particularly, to a composition suitable for topical application to prevent and treat periodontitis.

Description of the Prior Art

Periodontal disease is the major cause of tooth loss in adults. The periodontium is subject to inflammation for many reasons, primary among them being the accumulation of plaque deposits under and above the gumline. These calcareous deposits of organic and mineral matter, which consist of microbial colonies growing in carbohydrate residues (from food), attach themselves to tooth surfaces and can, over time, calcify into tartar. This hard, mineralized substance adheres tenaciously to the teeth and, when under the gumline, causes inflammation of the periodontium. Other causes of periodontitis can include malocclusion, food impaction and mouth breathing.

Periodontitis can cause the gumline to retract due to supporting bone loss and the gums to bleed, and eventually, if not treated, can result in tooth loss. Until now, the only known treatment for periodontitis, outside of taking preventive measures to keep it from developing in the first place, was surgery. The accepted surgical procedure involves removing the inflamed gum

tissue, which is expensive and requires a long and painful recovery.

There have been various attempts at treating periodontal disease without such surgical intervention. The best such attempt to date resides in an oral rinse sold by Procter & Gamble under the name Peridex®. The chemistry of this product is described in the 1988 Physicans' Desk Reference at pages 1648-49. Unfortunately, Peridex® rinse has not proved as efficacious against periodontal disease as might be desired and exhibits unwanted side effects, such as staining of tooth surfaces.

The following patents also disclose oral treatment agents, but none is believed to represent a substitute for surgical intervention as a treatment for periodontal disease:

Re.31,397	4,213,961
2,684,924	4,332,791
3,887,712	4,339,430
3,925,543	4,454,110
3,937,807	4,486,404
3,957,967	4,569,837
4,051,234	4,601,900
4,067,962	4,661,342
4,198,392	

Of interest with regard to the present invention are U.S. Patent 4,486,404 which, in Example 5, discloses a toothpaste containing chlorhexidine gluconate and allantoin, U.S. Patents 3,937,807 and 4,051,234, which disclose mouthwashes with gluconates and anti-stain agents, and U.S. Patent 4,569,837, which discloses the use of chlorhexidine gluconate and aspirin to treat periodontal disease.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide a composition and method for treating Periodontitis I without costly and painful surgical intervention.

In accordance with one aspect of the invention, a composition suitable for treating periodontitis comprises an aqueous solution of an antimicrobial agent with bacteriacidal activity, an agent with therapeutic action against skin ulcers, an analgesic, a stain remover and, if desired, suitable wetting agents, emulsifiers, dispersants, buffers stabilizers, preservatives, flavoring and coloring.

In accordance with another aspect of the invention, the composition is used in a treatment method which comprises the steps of topically applying the composition to inflamed periodontium.

DESCRIPTION OF PREFERRED EMBODIMENTS

In a preferred embodiment of the invention the various components of the composition of the present invention are present in an aqueous carrier of sterile distilled water, glycerine and ethanol. The glycerine provides the composition with the desired feel and texture and the ethanol acts as an antiseptic.

To this water-glycerine-ethanol carrier is added (1) chlorhexidine gluconate (0.12% solution), $C_{34}H_{54}Cl_2N_{10}O_{14}$ (Merck Index 2057), as an antimicrobial agent with bacteriacidal action, (2) allantoin, or (2,5-dioxo-4-imidazolidinyl)urea (Merck Index 242) as an agent that

exhibits therapeutic action against skin ulcers, (3) sodium salicylate, or 2-hydroxybenzoic acid monosodium salt (Merck Index 8515), as an analgesic, and (4) sodium bicarbonate (Merck Index 8414) as a stain remover, along with wetting agents, preservatives, emulsifiers, dispersants, buffers stabilizers, flavoring and coloring, as desired. (All references herein to the Merck Index refer to the 1983 edition.)

In particularly preferred embodiment, the above ingredients are provided in the following proportions:

TABLE 1

Sterile Water	70.77%
Glycerine (MI 4347)	11.15%
Ethanol (MI 212)	7.50%
Polysorbate 80 (as an emulsifier and dispersant; MI 7455)	4.20%
Chlorhexidine gluconate (0.12% sol.) (MI 2057)	3.50%
Sodium bicarbonate (as a stain remover; MI 8414)	0.50%
Sodium lauryl sulfate (as a wetting agent; MI 8474)	0.50%
Vanilla (as flavoring; MI 9732)	0.60%
Saccharine (as flavoring; MI 8170)	0.20%
Sodium salicylate (MI 8515)	0.15%
Allantoin (MI 242)	0.638%
Sodium benzoate (as a preservative; MI 8413)	0.10%

Xanthan gum (as a stabilizer and emulsifier; MI 9868)	0.10%
Sodium borate (as a buffer; MI 8421)	0.085%
F.D.& C. Blue (as coloring)	0.005%
F.D.& C. Red 40 (as coloring)	0.002%

[Notes to Table 1 - (1) All proportions of the above ingredients are v/v; (2) "MI" refers to the Merck Index]

The above composition is prepared by first measuring an appropriate quantity of sterile distilled water; for example, 1000cc of the composition is to be prepared, 707.7cc of water are used. The remaining ingredients are added in the order listed in Table 1, with each ingredient being thoroughly mixed by gently stirring the composition before the next ingredient is added.

A clinical test involving 30 people was performed using a composition similar to that set out above, except for using 72.77% sterile water, 8.00% ethanol, 1.50% chlorhexidine gluconate (0.12% solution) and 0.138% allantoin. The subjects were chosen because all exhibited periodontal pockets up to 8mm or 9mm deep. Prior to beginning the treatment regimen, all 30 subjects agreed not to brush or floss their teeth for one week. Then, 15 of the subjects rinsed their mouths three times a day with 1.0 cc of the above composition 30 seconds before brushing and 15 rinsed their mouths three times a day with an equal amount of a colored sugar-water placebo 30 seconds before brushing. The subjects did not know whether they were using the inventive composition or the placebo.

Once a week the teeth of each subject were checked for the presence of plaque using a commercially available plaque-disclosing solution, Superdent® disclosing solution

concentrate, made by Rugby Laboratories, Inc., of Rockville Centre, Long Island, NY 11570. All subjects using the inventive composition showed little or no plaque accumulation, while there was such plaque accumulation on the teeth of the subjects using the placebo.

The test procedures were continued for 12 weeks, and the subjects' conditions were measured in accordance with the Simplified Oral Hygiene Index (OHI-S) described in Orban's Periodontics (3rd Ed. 1968), The C.V. Mosby Co., St. Louis, MO, at page 134. It was found that the average OHI-S for the subjects on the placebo went from 8mm to 9mm periodontal pocket depth to 6mm to 8mm pocket depth during the 12 week test, while that for the subjects using the inventive composition improved from 8mm to 9mm periodontal pocket depth to 2mm or 3mm pocket depth, which is considered within normal range.

It is expected that repeated use of the inventive solution will reduce inflammation, stop bleeding and keratenize damaged periodontal tissue.

Of course, variations of the above preferred embodiment are possible within the scope of the present invention, such as varying the proportions of the chlorhexidine gluconate, allantoin and sodium salicylate within ranges that provide efficacious results. It is intended by the claims appended below to include all such variations within the present invention.

WHAT I CLAIM IS:

1. A composition for treating periodontal disease comprising an aqueous carrier having therein chlorhexidine gluconate, allantoin and sodium salicylate.

2. A composition according to claim 1, further comprising a stain remover.

3. A composition according to claim 2, wherein said stain remover is sodium bicarbonate.

4. A composition according to claim 1, wherein said chlorhexidine gluconate is present as a 0.12% solution and said aqueous carrier consists essentially of sterile water, glycerine and ethanol.

5. A composition for treating periodontal disease consisting essentially of the following ingredients in the following amounts according to volume:

Sterile Water	70.77%
Glycerine	11.15%
Ethanol	7.50%
Polysorbate 80	4.20%
Chlorhexidine gluconate (0.12% sol.)	3.50%
Sodium bicarbonate	0.50%
Sodium lauryl sulfate	0.50%
Sodium salicylate	0.15%
Allantoin	0.638%

Xanthan gum	0.10%
Preservatives, buffers, flavoring and coloring	0.992%

6. A method for treating periodontal disease comprising the steps of:

providing a composition including an aqueous carrier having therein chlorhexidine gluconate, allantoin and sodium salicylate; and

applying said composition topically to a human periodontium.

7. A method according to claim 5, wherein the composition further includes a stain remover.

8. A method according to claim 6, wherein the stain remover is sodium bicarbonate.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US90/01041

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC (5): A61K 7/16, 7/22; C11D 3/48
US 424/49; 514/900,635,165; 252/106

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
U.S.	424/49;514/900,635,165;252/106

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X Y	WO, A, 87/05501, 24 September 1987, (GOLDEMBERG), see page 11, lines 21-37; page 12.	1-3,6-8 1-12
Y	US, A, 4,512,968, 23 April 1985, (KOMIYAMA et al.), see col.3, lines 40-68; examples	1-12
Y	US, A, 4,370,314, 25 January 1983, (GAFFAR) see col.2, lines 1-4; col.3, lines 30-68; examples	1-12
Y	US, A, 4,454,110, 12 June 1984, (CASLAVSK et al.) see col.4, lines 11-68; examples	1-12
Y	EP, A, A0130690, 01 September 1985, (SUZUKI et al.), see page 6, lines 21-38, page 7, lines 1-38; page 9, lines 16-26.	1-12

* Special categories of cited documents: [10]

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
11 APRIL 1990	15 MAY 1990
International Searching Authority	Signature of Authorized Officer
ISA/US	CARMEN B. PILI-CURTIS

Form PCT/ISA/210 (second sheet) (Rev.11-87)